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On page 60, please replace the paragraph beginning at line 33 with the following paragraph:

Q 11 Bst NI fingerprinting (Marks et al., 1991, J. Mol. Biol. 222(3):581-597) of the 28 positive clones revealed a total of seven different patterns in the pool.(Figure 25). All seven clones recognized GPVI on transduced cells stained in a flow cytometry assay (Figures 26A-26I). Suggesting that the phage antibodies recognized native epitopes. The seven unique scFv's were subjected to small scale purification using Ni-chelate chromatography. Figure 27 shows the purity and yield of the scFvs as judged by coomassie staining on SDS-PAGE. The average scFv yield was around 10 ml/L with smaller shaker flask cultures (20 mL). Coomassie staining of SDS gels revealed a single dominant band migrating at approximately 30KDa, the expected molecular size of scFvs.

REMARKS

The specification has been amended to reflect the drawing designations provided for in the formal drawings. These amendments have been made in order to conform to the current Patent Office regulations regarding formal drawings. A marked up version of the paragraphs in the specification amended herein, with deletions and additions indicated by brackets and underlining, respectively, is attached hereto in Exhibit A. No new matter has been introduced by the above-made amendments.

Applicant respectfully requests entry of the above-made amendments and remarks.

Respectfully submitted,

Date: July 31, 2002

Laura A. Coruzzi 30,742
Laura A. Coruzzi (Reg. No.)

By: Muna Abu-Shaar
Muna Abu-Shaar
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PENNIE & EDMONDS LLP
1155 Avenue of the Americas
New York, New York 10036-2711
(212) 790-9090

Enclosures

EXHIBIT A
A MARKED UP VERSION OF PARAGRAPHS IN THE SPECIFICATION
OF U.S. APPLICATION SERIAL NO. 09/829,495
AMENDED ON JULY 31, 2002
(ATTORNEY DOCKET NO. 7853-234)

A marked up version of the replacement paragraph showing the changes made relative to the paragraph beginning on page 14, line 28 of the specification:

FIGURES [3A-3D] 3A-3C depict an alignment of the nucleotide sequence of the open reading frame for human monocyte inhibitory receptor precursor (SEQ ID NO:24; GenBank Accession Number U91928) and the nucleotide sequence of the open reading frame for human TANGO 268 (SEQ ID NO:2). The nucleotide sequences of coding regions of human monocyte inhibitory receptor precursor and human TANGO 268 are 37.7% identical. The nucleotide sequences of full-length, including the 5' and 3' untranslated regions (UTRs), human monocyte inhibitory receptor precursor SEQ ID NO:11; GenBank Accession Number U91928) and human TANGO 268 are 49.9% identical. These alignments were performed using the ALIGN alignment program with a PAM120 scoring matrix, a gap length penalty of 12, and a gap penalty of 4.

A marked up version of the replacement paragraph showing the changes made relative to the paragraph beginning on page 15, line 3 of the specification:

[FIGURES 4A-4B depict] FIGURE 4 depicts an alignment of the amino acid sequence of human monocyte inhibitory receptor precursor (SEQ ID NO:12) and the amino acid sequence of human TANGO 268 (SEQ ID NO:3). The amino acid sequences of human monocyte inhibitory receptor precursor and human TANGO 268 are 23.0% identical. This alignment was performed using the ALIGN alignment program with a PAM120 scoring matrix, a gap length penalty of 12, and a gap penalty of 4.

A marked up version of the replacement paragraph showing the changes made relative to the paragraph beginning on page 16, line 5 of the specification:

[FIGURES 9A-9B depict] FIGURE 9 depicts an alignment of the amino acid sequence of human monocyte inhibitory receptor precursor (SEQ ID NO:12) and the amino acid sequence of mouse TANGO 268 (SEQ ID NO:16). The amino acid sequences of

human monocyte inhibitory receptor precursor and mouse TANGO 268 are 20.3% identical. This alignment was performed using the ALIGN alignment program with a PAM120 scoring matrix, a gap length penalty of 12, and a gap penalty of 4.

A marked up version of the replacement paragraph showing the changes made relative to the paragraph beginning on page 19, line 34 of the specification:

[FIGURE 26] FIGURES 26A-26I: Coomassie staining of purified scFv's. scFv's were purified using Ni-chelate chromatography and the purity of the scFv's was confirmed by coomassie-stained SDS-PAGE.

A marked up version of the replacement paragraph showing the changes made relative to the paragraph beginning on page 27, line 23 of the specification:

[Figures 3A-3D] Figures 3A-3C show an alignment of the human TANGO 268 coding region (SEQ ID NO:2) with the human monocyte inhibitory receptor precursor protein coding region (SEQ ID NO:24). The human monocyte inhibitory receptor has been shown to downregulate activation responses by phosphatases. The nucleotide sequences of coding regions of human monocyte inhibitory receptor precursor and human TANGO 268 are 37.7% identical. The full-length nucleic acid sequence of human TANGO 268 (SEQ ID NO:1) exhibits 49.9% identity to the full-length nucleic acid human monocyte inhibitory receptor precursor (SEQ ID NO:11; Accession Number U91928).

A marked up version of the replacement paragraph showing the changes made relative to the paragraph beginning on page 27, line 31 of the specification:

[Figures 4A-4B show] Figure 4 shows that there is an overall 23% identity between the amino acid sequence of the human TANGO 268 protein and the amino acid sequence of the human monocyte inhibitory receptor protein (SEQ ID NO:12; Accession Number U91928).

A marked up version of the replacement paragraph showing the changes made relative to the paragraph beginning on page 30, line 27 of the specification:

In general, mouse TANGO 268 has most homology to various members of the immunoglobulin superfamily that includes NK inhibitory and activating receptors and Fc receptors. The full-length nucleic acid sequence of mouse TANGO 268 exhibits 35.6%

identity to the full-length nucleic acid human monocyte inhibitory receptor precursor (SEQ ID NO:11; Accession Number U91928). [Figure 8] Figures 8A-8B show an alignment of the mouse TANGO 268 coding region (SEQ ID NO:15) with the human monocyte inhibitory receptor precursor protein coding region (SEQ ID NO:24). The nucleotide sequences of the coding regions of human monocyte inhibitory receptor precursor and mouse TANGO 268 are 34.4% identical. The nucleotide sequences of the full-length human monocyte inhibitory receptor precursor (SEQ ID NO:11; Accession Number U91928) and full-length mouse TANGO 268 (SEQ ID NO:14) are 35.6% identical. Figure 9 show that there is an overall 20.3% identity between the mouse TANGO 268 amino acid sequence and the human monocyte inhibitory receptor protein amino acid sequence (SEQ ID NO:12; Accession Number U91928).

A marked up version of the replacement paragraph showing the changes made relative to the paragraph beginning on page 39, line 17 of the specification:

Transduced cells were analyzed by flow cytometry using FITC conjugated Cvx. As a control, we used FITC conjugated bothrojaracin, another snake venom protein structurally very close to Cvx but a pure thrombin inhibitor that does not bind to platelets. Transduction of murine 32D cells with a retrovirus expressing murine GPVI resulted in a strong Cvx-associated staining compared to cells transduced with the control virus, indicating that these cells express GPVI at their surface ([Figure 15] Figures 15A-15C). Similar results were obtained with FDC-P1, and Ba/F3 (all murine cell lines) and with K562 and U937, indicating that murine or human GPVI are expressed at the surface of all these cell lines after transduction. Cvx was found to bind to the wild type HEL cells but the binding was clearly increased after retroviral transduction indicating an increased expression in cells already constitutively expressing GPVI.

A marked up version of the replacement paragraph showing the changes made relative to the paragraph beginning on page 40, line 21 of the specification:

Two cell lines were tested: U937 and FDC-P1. Neither the cells expressing GPVI, nor the control cells bound to immobilized BSA. However, expression of recombinant human or mouse GPVI in U937 or FDCP-1, respectively, clearly promotes the adhesion of these cells to immobilized collagen and to a greater extent to immobilized Cvx ([Figure 16]

Figures 16A-16B). This result indicates that GPVI protein functions as a receptor for collagen I. In addition, GPVI is a receptor for collagen III.

A marked up version of the replacement paragraph showing the changes made relative to the paragraph beginning on page 43, line 5 of the specification:

rhusGPVI:Fc did not induce platelet aggregation or granule secretion by itself. When platelets were incubated with Cvx, addition of rhusGPVI:Fc (0.25 to 5 µg/ml) fully inhibited platelet aggregation and dense granule secretion ([Figure 18] Figures 18A-18B). In addition, when rhusGPVI:Fc was added to the platelet suspension prior to Cvx, it also inhibited aggregation and secretion, indicating that it could compete with platelet GPVI for Cvx (Figure 18 A). Incubation of collagen with rhusGPVI:Fc induces a loss in its ability to induce platelet aggregation and secretion (Figure 18 B). However, a tenfold higher concentration of rhusGPVI:Fc than required for Cvx was needed to produce this inhibitory effect. Furthermore, when recombinant soluble GPVI was added to platelets prior to collagen, no inhibition was observed (Figure 18 B). These results demonstrate that the extracellular domain of GPVI is active in blocking Cvx- and collagen-induced platelet aggregation.

A marked up version of the replacement paragraph showing the changes made relative to the paragraph beginning on page 60, line 33 of the specification:

Bst NI fingerprinting (Marks et al., 1991, J. Mol. Biol. 222(3):581-597) of the 28 positive clones revealed a total of seven different patterns in the pool.(Figure 25). All seven clones recognized GPVI on transduced cells stained in a flow cytometry assay ([Figure 26] Figures 26A-26I). Suggesting that the phage antibodies recognized native epitopes. The seven unique scFv's were subjected to small scale purification using Ni-chelate chromatography. Figure 27 shows the purity and yield of the scFvs as judged by coomassie staining on SDS-PAGE. The average scFv yield was around 10 ml/L with smaller shaker flask cultures (20 mL). Coomassie staining of SDS gels revealed a single dominant band migrating at approximately 30KDa, the expected molecular size of scFvs.